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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/489,667	01/19/00	DONOVAN S	D-2875

HM22/1220

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EXAMINER	
KAM, C	
ART UNIT	**PAPER NUMBER**
1653	9

DATE MAILED: 12/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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Office Action Summary	Application No.	Applicant(s)	
	09/489,667	DONOVAN, STEPHEN	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-66 is/are pending in the application.

4a) Of the above claim(s) 21-25 and 36-65 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-20,26-35,and 66 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims 1-66 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. Claim 26 is objected because an polypeptide agent is used. Appropriate correction is required.

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U. S. C. 121:

I. Claims 1-20, 26-35, and 66, drawn to proteins, classified in class 530, subclass 350.

II. Claims 21-25, 36, and 37, drawn to a method of making protein or polypeptide agent using recombinant DNA technique, classified in class 435, subclass 69.7 and 320.1.

III. Claims 38-65, drawn to a method of treating pain using protein agent, classified 514, subclass 2.

3. The inventions are distinct, each from the other because of the following reasons:

Inventions II and I are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the product as claimed may be isolated from its natural source or made by chemical peptide synthesis.

Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product

as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the protein as claimed can be used in a different process such as to assay or purify the cognate receptor of the protein, in assays for the identification of agonists or antagonists of the receptor protein, or as a reagent for *in vitro* assays. The process of invention III can be practiced with other drugs such as steroids, or opioids.

Invention II is distinct from Invention III because the method of II is not required for the method of III, and the method of III is not required for the method of II.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and recognized divergent subject matter, and because inventions I, II, and III require different searches but are not co-extensive, examination of these distinct inventions would pose a serious burden on the examiner and therefore restriction for examination purposes as indicated is proper.

After a telephone conversation with Quan Nguyen on 11/25/2000 and an e-mail message received on 11/27/2000, a provisional election was made with traverse to prosecute the invention of Group I, claims 1-20, 26-35, and 66. Affirmation of this election must be made by applicant in replying to this Office action. Claims 21-25, and 36-65 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-10, 12-13, 15-19, and 26-34 are rejected under 35 U.S.C. 112, first paragraph.

Claims 1-10, 12-13, 15-19, and 26-34 are rejected because the specification, while being enabling for an agent or a polypeptide agent comprising a transmission compound, substance P as the targeting moiety, does not reasonably provide enablement for an agent or a polypeptide agent comprising any transmission compound as the targeting moiety. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-10, 12-13, 15-19, and 26-34 are drawn to encompass an agent or a polypeptide agent containing any transmission compound (claims 1-10, 18-19, and 26-34), any peptide (claim 12), any member in the tachykinin family (claim 13), any precursor of substance P (claim 15), any fragment of substance P (claim 16), or any substance P analog (17) as the targeting moiety. The specification, however, only discloses cursory conclusions (see pages 15-21), without data (see pages 21-31, 36-38) to support the findings, which states that an agent containing a light chain of botulinum toxin A or B, an N-terminal segment of heavy chain of botulinum toxin A and substance P can be used for treating pain. There is no disclosure or description of an agent containing any other transmission compound than substance P as the targeting moiety. Despite knowledge in the art for transmission compound, the claims encompass enormous numbers of transmission compounds as the targeting moiety of an agent, which would not be expected by the skilled artisan to accomplish the goal set forth. Thus, the claims are directed to specifically encompass enormous numbers of embodiments for which it is not expected to be known a priory whether the embodiments are in the same manner as substance P inoperative or operative. Since it is not routine in the art to engage in *de novo* experimentation

where the expectation of success is unpredictable, the skilled artisan would require additional guidance in order to make and use such agent in a manner reasonably commensurate with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

5. Claims 26-35 are rejected under 35 U.S.C. 112, first paragraph.

Claims 26-35 are drawn to encompass any polypeptide agent comprising a first amino acid sequence region with a transmission compound as the first domain and a translocation element as the second domain as well as a second amino acid sequence region containing a therapeutic element. The specification, however, only discloses cursory conclusions, without data to support the findings, which states that a polypeptide agent containing a light chain of botulinum toxin A or B, an N-terminal segment of the heavy chain of botulinum toxin A and substance P can be used for treating pain. There is no disclosure or description of any other polypeptide agent than the two cited polypeptides. Since it is not routine in the art to engage in *de novo* experimentation where the expectation of success is unpredictable, the skilled artisan would require additional guidance in order to make and use such botulinum toxins in a manner reasonably commensurate with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the scope of the claims, unpredictability in the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-20, and 26-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite, because of the use of the term "derived from" therein. The term "derived from" renders the claim indefinite, it is not clear either in the specification or the claim that how many amino acids have been deleted, modified, or replaced as compared to the amino acid sequence from which it is derived. Claims 1, 26, and claims dependent there to are indefinite because it is not apparent what compounds would be "substantially similar". In claim 2, "can be" is only a latent capacity, a clearer recitation such as "is" is suggested.

7. Claims 4, 10, and 11 are rejected as being indefinite because of the use of the term "and mixtures thereof". Note that Markush groups must be closed and "and mixtures thereof" is open language in regard to the number of components and amounts of each in the mixtures.

8. Claim 5 is rejected as being indefinite because of the use of the term "at least one of a heavy chain, a fragment of a heavy chain, a light chain and a fragment of a light chain". The term "at least one of a heavy chain, a fragment of a heavy chain, a light chain and a fragment of a light chain" renders the claim indefinite, it is not clear in the claim that what kind of the clostridial neurotoxin component is.

9. Claim 17 is rejected as being indefinite because of the use of the term "analogues". The term "analogues" renders the claim indefinite, it is not clear either in the specification or the

claim that what kind of substance P analogues comprising at least one D-amino acid or a disulfide bridge.

10. Claims 9 and 19 are rejected as being indefinite because of the use of the term "one or more spacer components". The term "one or more spacer components" renders the claim indefinite, it is not clear either in the specification or the claim that how many spacer components are linked between the light chain (or a fragment of a light chain) and a heavy chain (or a fragment of a heavy chain).

11. Claims 3, 16, and 27 are rejected as being indefinite because of the use of the term "derivatives and fragments". The term "derivatives and fragments" renders the claim indefinite, it is not clear in the claim that what kind of derivatives and fragments of neurotoxins are. Use of the term "functional derivatives and fragments" would overcome the rejection.

12. Claim 34 is rejected as being indefinite because the claimed polypeptide contains a clostridial neurotoxin light chain as the second domain, which has a proteolytic activity and is different from the one in claim 26. In claim 26, the second domain of the polypeptide comprises a translocation element.

13. Claim 66 is unclear as to item (a) which is ambiguous as to what the proteolytic domain is attached and whether or not items (b) and (c) are attached to item (a). It is also not apparent whether or not the "attached" is covalent or non-covalent.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1-9, 12, 18-19, 26-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Foster *et al.* (WO96/33273) which teaches an agent containing a modified clostridial neurotoxin (a light chain, a fragment of the light chain, or a fragment of the light chain coupled to the N-terminal segment of heavy chain) covalently linked to a targeting moiety, a neuropeptide (see pages 12-16; page 24, Table 1; claims 25, 30) for treating pain.

Claim Rejections - 35 USC § 102

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

15. Claims 1-9, 12, 18-19, 26-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Foster *et al.* (US Patent 5,989,545) which teaches an agent containing a modified clostridial neurotoxin (a light chain, a fragment of the light chain, or a fragment of the light chain coupled to the N-terminal segment of heavy chain) covalently linked to a targeting moiety, a neuropeptide (see columns 7-8; Table 1; claims 17, 21) for treating pain.

Conclusion

16. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. Patent Examiner

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December 16, 2000

Christopher S. F. Low

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